

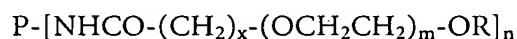
## CLAIMS

1. A method of treating disturbances in iron distribution in a patient suffering from heart disease comprising administering a therapeutically effective amount of human erythropoietin.
2. The method of claim 1, wherein the patient is suffering from heart insufficiency.
3. The method of claim 1, wherein the erythropoietin protein is epoetin alfa or epoetin beta.
4. The method of claim 1, wherein the erythropoietin protein has the amino acid sequence of SEQ ID NO:1.
5. The method of claim 1, wherein the erythropoietin protein has the sequence of human erythropoietin modified by the addition of from 1 to 6 glycosylation sites.
6. The method of claim 1, wherein the erythropoietin protein is darbepoetin alfa.
7. The method of claim 1, wherein the erythropoietin protein is pegylated.
8. The method of claim 7, wherein the erythropoietin protein is a conjugate, said conjugate comprising an erythropoietin protein having at least one free amino group and having the *in vivo* biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells and selected from the group consisting of human erythropoietin and analogs thereof which have a sequence of human erythropoietin modified by the addition of from 1 to 6 glycosylation sites or a rearrangement of at least

one glycosylation site; said erythropoietin protein being covalently linked to n poly(ethylene glycol) groups of the formula  $-\text{CO}-(\text{CH}_2)_x-(\text{OCH}_2\text{CH}_2)_m-\text{OR}$  with the  $-\text{CO}$  of each poly(ethylene glycol) group forming an amide bond with one of said amino groups; wherein R is lower-alkyl; x is 2 or 3; m is from about 450 to about 900; n is from 1 to 3; and n and m are chosen so that the molecular weight of the conjugate minus the erythropoietin protein is from 20 kilodaltons to 100 kilodaltons.

9. The method of claim 8, wherein x is 2, m is from about 650 to about 750, n is 1 and R is methyl.

10. The method of claim 8 wherein the conjugate has the formula



wherein

P is the residue of the erythropoietin protein without the free amino group that forms the amide linkage;

R is lower alkyl;

x is 2 or 3;

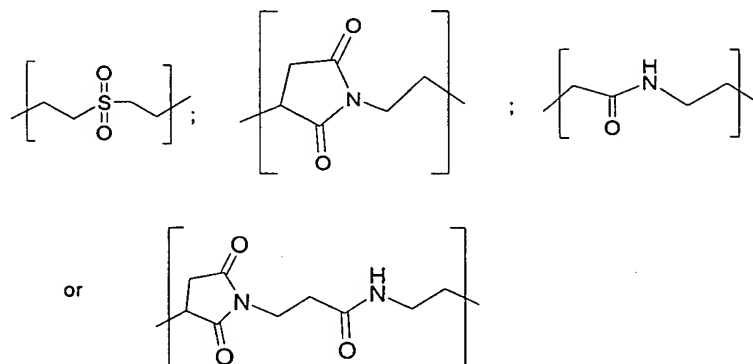
m is from about 450 to about 900; and

n is from 1-3;

and wherein m and n are selected such that the molecular weight of the conjugate minus the erythropoietin protein is from about 20 kd to about 100 kd.

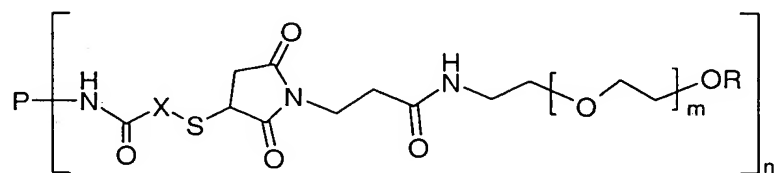
11. The method of claim 7, wherein the erythropoietin protein is a conjugate, said conjugate comprising an erythropoietin protein having at least one free amino group and having the *in vivo* biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells and selected from the group consisting of human erythropoietin protein and analogs thereof which have the primary structure of human erythropoietin protein modified by the addition of from 1 to 6 glycosylation sites; said erythropoietin protein being covalently linked to from one to three lower-alkoxy poly(ethylene glycol) groups, each poly(ethylene glycol) group being covalently linked to the erythropoietin protein *via* a linker of the formula  $-\text{C}(\text{O})-\text{X}-\text{S}-\text{Y}-$

with the C(O) of the linker forming an amide bond with one of said amino groups, X is  $-(CH_2)_k-$  or  $-CH_2(O-CH_2-CH_2)_k-$ , k is from 1 to 10, Y is



the average molecular weight of each poly(ethylene glycol) moiety is from about 20 kilodaltons to about 40 kilodaltons, and the molecular weight of the conjugate is from about 51 kilodaltons to about 175 kilodaltons.

12. The method of claim 11, wherein the erythropoietin conjugate has the formula:



wherein n is an integer from 1 to 3; m is an integer from 450 to 900; R is lower-alkyl; X is  $-(CH_2)_k-$  or  $-CH_2(O-CH_2-CH_2)_k-$ , k is 1 to 10 and P is the residue of the erythropoietin protein without the n amino groups which form an amide linkage with X.

13. The method of claim 1 wherein the amount of human erythropoietin administered to the patient is from about 100 U/kg to about 200 U/kg twice per week.

14. The method of claim 10 wherein the amount of the human erythropoietin administered to the patient is about 200 U/kg once every three weeks.